Supplemental Document

Biomedical Optics EXPRESS

In vivo test-driven upgrade of a time domain multi-wavelength optical mammograph: supplement

GIULIA MAFFEIS,[1,*] EDOARDO FEROCINO,[1] ALBERTO DALLA MORA,[1] ANTONIO PIFFERI,[1,2] RINALDO CUBEDDU,[1] AND PAOLA TARONI[1,2]

[1] *Politecnico di Milano, Department of Physics, Piazza Leonardo da Vinci, 32, 20133, Milan, Italy*
[2] *CNR-Istituto di Fotonica e Nanotecnologie, Piazza Leonardo da Vinci, 32, 20133, Milan, Italy*
[*] *giulia.maffeis@polimi.it*

Supplement DOI: https://doi.org/10.6084/m9.figshare.13607120

Parent Article DOI: https://doi.org/10.1364/BOE.412210

In vivo test-driven upgrade of a time domain multi-wavelength optical mammograph: supplemental document

This supplementary document aims at giving further information about the results of the linearity assay for the optical mammograph described in the main paper. The linearity assay is one of the tests contributing to the standardized performance assessment protocol for photon migration instruments, known as MEDPHOT [1].

The main article defines linearity (Section 2.3) and illustrates the results obtained for a single wavelength (*i.e.* 785 nm), for both the initial instrument set-up (employing the Surface Concept Time-to-Digital Converter, SC TDC) (Fig. 4, Section 3.3) and the *in vivo* test-driven upgrade (which instead uses the MultiHarp TDC from PicoQuant, MH) (Fig. 5).

Here, we want to depict a more complete picture of the linearity assay by synthetically reporting the average results over the 7 wavelengths available in our optical mammograph (namely 635, 680, 785, 905, 930, 975, 1060 nm) for both set-up versions. This way, we can compare their average behavior.

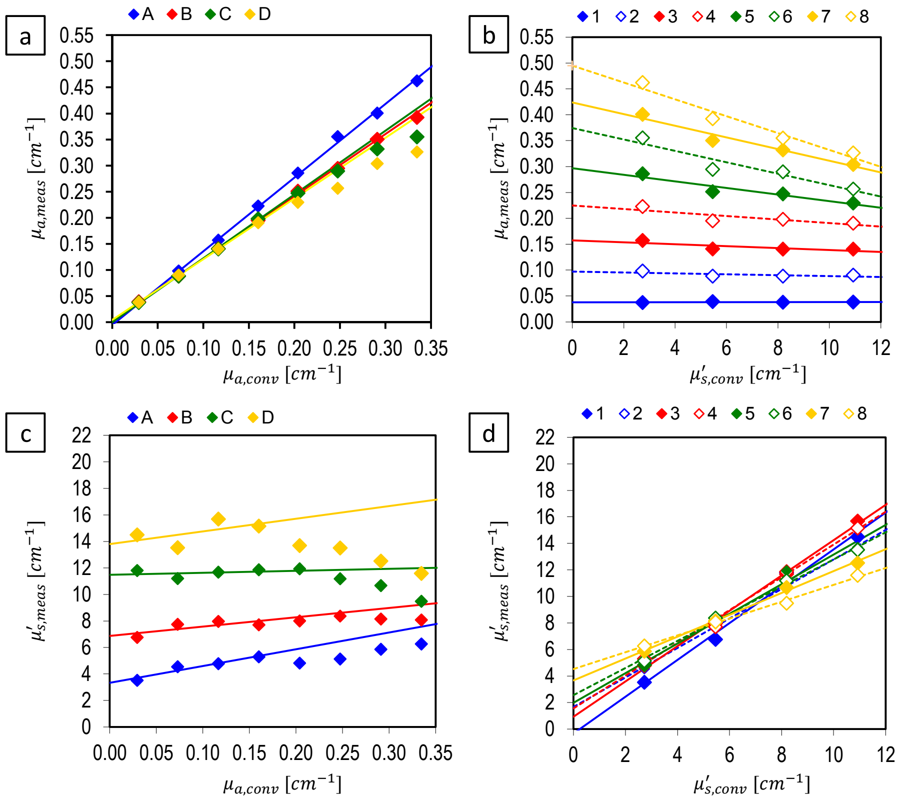

Fig. S1. Results for the linearity assay averaged over the 7 wavelengths for the initial instrument set-up with the SC TDC.

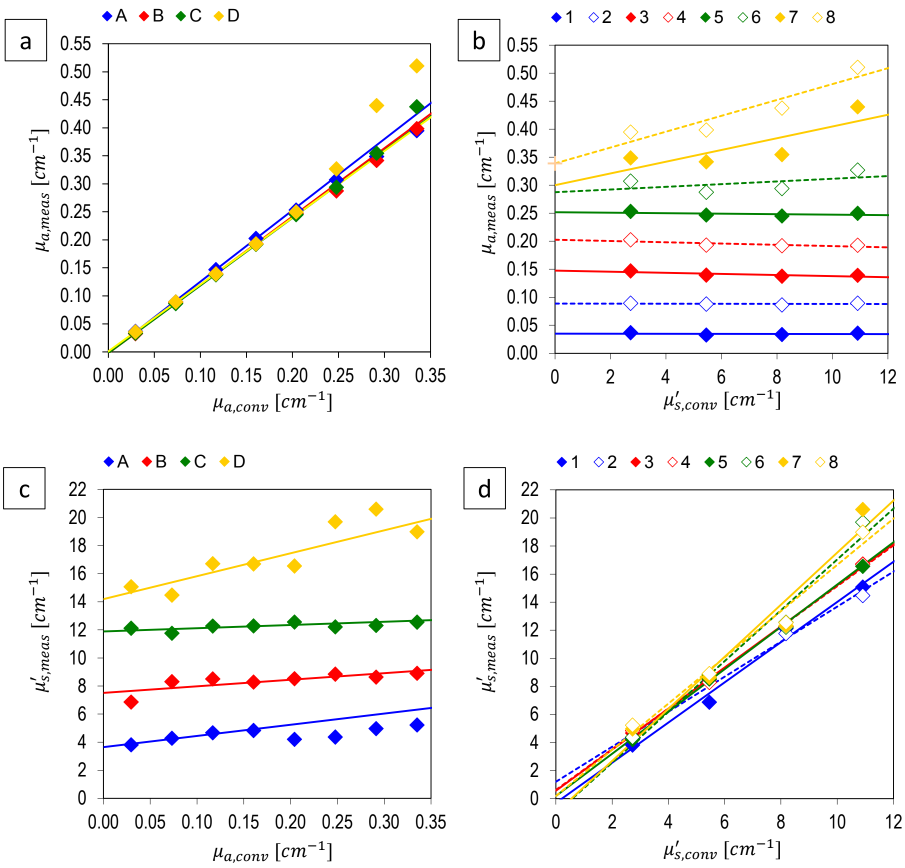

Fig. S2. Results for the linearity assay averaged over the 7 wavelengths for the upgraded set-up with the MH TDC.

Fig. S1 and Fig. S2 report the linearity results averaged over all the 7 wavelengths for the initial instrument version and the upgraded one, respectively. Corresponding plots have the same axis extension for an easier comparison. Letter (number) sequences represent increasing values of the conventionally true reduced scattering μ'_s (absorption μ_a) coefficient. For a detailed description of the plots' meaning and legend, reference is made to Sections 2.3 and 3.3 of the main paper. Briefly, comparing Fig. S1 and Fig. S2 an overall improvement, even if not drastic, emerges immediately.

Contrary to Fig. S1 a), in Fig. S2 a) series A ($\mu'_s = 5\ cm^{-1}$) is closer to the others (B, C, D), in fact its angular coefficient reduces from $m_{A,SC} = 1.41$ to $m_{A,MH} = 1.27$, suggesting lower sensitivity of the absorption estimate to low scattering. In Fig. S2 b) lines are fairly horizontal ($|m|$ <0.003) up to series 6 ($\mu_a = 0.25\ cm^{-1}$), while a slope can be inferred already for series 4 in Fig. S1 b) due to a negative absorption-to-scattering coupling. Also in Fig. S2 c) lines are more horizontal than the SC-TDC counterparts, except for the D series, and data are less scattered. The comparison between the average angular coefficients over series A, B and C reads $m_{ABC,SC} = 7.05$ *vs* $m_{ABC,MH} = 4.98$, suggesting a limited scattering-to-absorption coupling. $m_{D,SC} < m_{D,MH}$ only because the linear interpolation is based on the first 4 points of each series. Finally, in Fig. S2 d) the lines' intercept spread is smaller: q_{SC} ranges from -0.34 to 4.52, while q_{MH} from -1.06 to 1.20.

While Fig. S1 and Fig. S2 report the average value of μ_a and μ'_s over wavelengths, Table S1 and Table S2 present the corresponding standard deviations σ_a and σ'_s, respectively for the first and the second version of the instrument. In particular, $\sigma_{a,meas}$ and $\sigma'_{s,meas}$ are related to the measured values, while $\sigma_{a,conv}$ and $\sigma'_{s,conv}$ to the conventionally true values, taken as reference. The two tables show very similar behavior, except for the bottom right corner of the table (high absorption and high scattering), thus in compliance with the observations on the previous plots.

Table S1. Standard deviations over wavelengths of absorption and reduced scattering coefficients, measured with the SC-TDC set-up. Values in cm^{-1}.

$\sigma'_{s,conv}$		0.96		1.91		2.87		3.83	
		A		B		C		D	
$\sigma_{a,conv}$		$\sigma_{a,meas}$	$\sigma'_{s,meas}$	$\sigma_{a,meas}$	$\sigma'_{s,meas}$	$\sigma_{a,meas}$	$\sigma'_{s,meas}$	$\sigma_{a,meas}$	$\sigma'_{s,meas}$
0.03	1	0.03	0.73	0.03	1.71	0.03	3.01	0.03	3.56
0.02	2	0.02	0.95	0.02	1.96	0.02	2.72	0.02	3.15
0.01	3	0.02	1.01	0.02	2.02	0.02	2.83	0.01	3.73
0.01	4	0.02	1.08	0.01	1.86	0.01	2.80	0.01	3.48
0.02	5	0.02	0.88	0.01	1.89	0.02	2.85	0.01	2.63
0.03	6	0.03	0.94	0.02	1.98	0.02	2.70	0.06	3.66
0.03	7	0.03	1.22	0.03	1.96	0.04	2.59	0.06	3.07
0.04	8	0.04	1.27	0.05	2.03	0.08	2.67	0.08	2.91

Table S2. Standard deviations over wavelengths of measured absorption and reduced scattering coefficients, measured with the MH set-up. Values in cm^{-1}.

$\sigma'_{s,conv}$		0.96		1.91		2.87		3.83	
		A		B		C		D	
$\sigma_{a,conv}$		$\sigma_{a,meas}$	$\sigma'_{s,meas}$	$\sigma_{a,meas}$	$\sigma'_{s,meas}$	$\sigma_{a,meas}$	$\sigma'_{s,meas}$	$\sigma_{a,meas}$	$\sigma'_{s,meas}$
0.03	1	0.03	0.78	0.02	1.57	0.02	2.93	0.02	3.41
0.02	2	0.02	0.88	0.02	1.89	0.02	2.60	0.02	3.16
0.01	3	0.02	1.02	0.01	1.88	0.01	2.69	0.01	3.80
0.01	4	0.02	0.99	0.01	1.73	0.01	2.63	0.02	4.25
0.02	5	0.02	0.78	0.01	1.76	0.03	3.14	0.05	5.42
0.03	6	0.02	0.80	0.02	1.89	0.05	3.69	0.11	9.41
0.03	7	0.02	0.91	0.03	1.96	0.11	4.83	0.23	12.25
0.04	8	0.02	0.94	0.08	2.62	0.18	6.04	0.28	12.58

Finally, as we stated in the main paper, the behavior of a single wavelength is representative of all the others. In fact, the average graphs of Fig. S1 recall the ones for λ = 785 nm shown in Fig. 4 in the main paper and, analogously, Fig. S2 resembles Fig. 5.

In conclusion, the optical mammograph benefited from the hardware upgrade at every level, substantially in *in vivo* measurements, significantly in basic performance key features.

References

1. A. Pifferi, A. Torricelli, A. Bassi, P. Taroni, R. Cubeddu, H. Wabnitz, D. Grosenick, M. Möller, R. Macdonald, J. Swartling, T. Svensson, S. Andersson-Engels, R. L. P. van Veen, H. J. C. M. Sterenborg, J.-M. Tualle, H. L. Nghiem, S. Avrillier, M. Whelan, and H. Stamm, "Performance assessment of photon migration instruments: the MEDPHOT protocol," Appl. Opt. **44**(11), 2104 (2005).